My name is Dr. Charles King. I am a former assistant professor of marketing at Harvard University and I am an economist with Greylock McKinnon Associates, an economic consulting firm in Cambridge, Massachusetts. I received a law degree from Yale in 1979 and a Ph.D. from MIT in 1997. Since then, my work has focused on the analysis of marketing practices and their effects on sales by a variety of companies including those of pharmaceutical companies. I have successfully applied economic and marketing theories to the pharmaceutical industry in multiple litigation matters and in my academic research.

Today, I am here to talk to you about the marketing practices undertaken by Warner-Lambert and Pfizer to promote Neurontin and the effects those practices had on the sales of Neurontin. Specifically, I will testify to the following four areas that Mr. Lanier talked about in his opening statements:

- Were the marketing and promotional efforts of Warner-Lambert and Pfizer significant contributing factors to the unapproved or off-label sales of Neurontin?
- Would significant off-label sales of Neurontin have continued had Pfizer stopped its off-label promotional activities for Neurontin?
- Did Warner-Lambert's and Pfizer's off-label marketing of Neurontin directly or indirectly influence all, or substantially all, physicians who prescribed Neurontin?

- Did the suppression of information about the serious adverse side-effects of Neurontin enable the growth of unapproved or off-label sales for Neurontin?

Based upon my analysis and my experience, as an expert in marketing, I conclude the following:

[Slide 1]

- First, the marketing and promotional efforts of Warner-Lambert and Pfizer were significant contributing factors to the unapproved or off-label sales of Neurontin;
- Second, significant off-label sales of Neurontin would have continued had Pfizer, after acquiring Warner-Lambert, discontinued off-label promotional activities for Neurontin;
- Third, Pfizer's off-label marketing of Neurontin directly or indirectly influenced all, or substantially all, physicians prescribing of Neurontin; and
- Finally, suppression of the information regarding serious adverse events enabled the growth of Neurontin's off-label sales.

In forming my opinions, I have applied basic scientific methods commonly employed in economic and marketing research in addressing these types of issues. Specifically, I systematically reviewed strategic documents, financial records, testimony and relevant academic research relating to the issues at hand. I will present the supporting evidence for these opinions. But first, let me provide some background relevant to the issues raised in this litigation.

Neurontin is a prescription drug that was approved by the Food and Drug Administration, the FDA, in December 1993. **[Slide 2]** The FDA approves all prescription drugs for specific indications or uses before they are sold to the public. Neurontin was approved for the adjunctive treatment of partial seizures in people older than 12 with epilepsy. This means that Neurontin was approved only as a second-line or add-on treatment for use in conjunction with another front-line epilepsy drug. Neurontin was not approved for any other use at that time, not for pain, not for migraines, not for bipolar and not for any other indication aside from adjunctive treatment for epilepsy. Neurontin was not approved for dosages exceeding 1800 mg per day. In 2000, the FDA approved Neurontin as adjunctive therapy for seizures in children and in 2002 for the management of post-herpetic neuralgia. These are the only FDA-approved uses of Neurontin. **[Slide 3]** Following FDA approval in 1993, Parke-Davis, a division of Warner-Lambert, began selling Neurontin in January 1994.

The number of people in this country with epilepsy is small and sales of Neurontin would be limited by that if it was only sold for its approved uses. This fact was evident to Warner-Lambert. By 1995, Warner-Lambert had analyzed the prospects for Neurontin if marketed only for approved uses and estimated its lifetime future sales would add up to only $500 million. While $500 million seems like a lot of money, it is only a fraction of the total amount of sales actually generated by Neurontin. Actual sales for Neurontin were more than $10 billion. So, the question is, how did a drug with such limited approval and sales prospects grow to a $10 billion drug? The answer is quite simple, Warner-Lambert undertook an extensive plan to market Neurontin for uses for which it was not approved; Warner-Lambert marketed Neurontin for off-label uses.

It is interesting to note that Warner-Lambert pled guilty to felony charges of illegally promoting Neurontin for off-label uses and failing to provide doctors with adequate instructions for the safe prescribing of Neurontin off-label. Events specified in the guilty plea took place in Warner-Lambert's Southeast Customer Business unit, which includes the state of Tennessee, as well as other parts of the country. Warner-Lambert unequivocally admitted to a variety of charges including:

- Marketing Neurontin for off-label uses including pain, bipolar and other unapproved uses;
- Using sales representatives and medical liaisons to improperly promote Neurontin off-label; and
- Paying doctors to promote off-label uses of Neurontin including payments for such things as trips, luxury hotels and even tickets to the Olympics.

To settle these criminal charges, Warner-Lambert paid a total of $430 million in criminal fines and reimbursements. Again, $430 million sounds like a lot of money, but it was only a small fraction of the total amount of Neurontin sales that resulted from their illegal off-label marketing activities.

The words "off-label" have been and will be heard a lot in this trial. Let's take a minute to talk about what those words mean. As mentioned above, the FDA approves drugs for specific uses which appear on its official label. A drug company can only market the drug for its approved uses. Neurontin could only be marketed for its approved uses. However, doctors have the discretion to use FDA-approved drugs anyway that they perceive is useful to their patients regardless of their approved uses.

Warner-Lambert and Pfizer took advantage of this and marketed Neurontin for off-label uses including pain and psychiatric disorders.

After evaluating the potential markets for other clinical uses, such as treatment of chronic pain and bipolar disorder, Warner-Lambert calculated that seeking FDA approval would not be worthwhile because of the expense of clinical trials, the short remaining patent life for Neurontin and the potential adverse impact on the sales of a new drug that Warner-Lambert was developing. Warner-Lambert decided instead to promote off-label uses of Neurontin even though off-label promotion is expressly prohibited by the FDA.

Prescription drugs are not like ordinary consumer goods. People depend on them for their health and, in some cases, even their life. Unlike typical consumer goods, prescription drugs can only be purchased under the supervision of a physician. Although patient preferences play a role, doctors exercise primary influence over health-care decisions, particularly for serious medical conditions. Doctors, as learned intermediaries, select the best drug for the patient. Since doctors ultimately decide which drugs to prescribe, pharmaceutical companies concentrate their marketing efforts on them. The goal is to influence doctors' prescribing habits to increase drug company profits.

Given the pace of technological innovation and new treatments in modern medicine, physicians must keep abreast of a continuous stream of new medical developments. Where do doctors get their information on which drugs to prescribe for their patients? Physicians look to a variety of sources for information. For example,

published medical literature, conferences, meetings, continuing medical education (CME) events, opinion leaders and other colleagues in the field.

Drug companies also provide information to physicians and spend a large percentage of their revenues on marketing. Pharmaceutical firms typically spend as much, or more, on marketing than they do on research and development. Both Warner-Lambert and Pfizer spent more on promoting their drugs than they did on research and development.

Drug companies employ a variety of marketing tools to promote their products to physicians, including personal selling (or "detailing"), direct mail, medical journal advertising, free samples to physicians and medical education events. Drug company sales representatives visit doctors in their offices and hospitals to promote their products and inform doctors about new medicines, products and therapies. Studies have shown that physicians are directly influenced by information provided by pharmaceutical representatives.

The distribution of free drug samples ("sampling") also targets doctors directly. Sampling is designed to increase sales by building a physician's personal experience with the drug and increasing his or her confidence in prescribing it.

Studies have demonstrated the positive effect of drug promotion and company-sponsored continuing medical education events on drug prescriptions. These events include symposia, conferences, and lectures, all of which influence prescribing behavior.

Looking to the evidence in this case, we see that the strategy for the marketing and promotion of Neurontin for off-label uses was sophisticated, comprehensive and

well coordinated. In the years following Neurontin's initial approval, Warner-Lambert and Pfizer implemented strategies to promote Neurontin for a variety of off-label uses including pain, psychiatric disorders and at doses of more than 1800 mg per day. In each case, off-label Neurontin prescriptions sharply increased after the commencement of off-label marketing campaigns. These strategies included drug company representatives, medical liaisons, and continuing medical education events. In 1994, before Warner-Lambert undertook its off-label marketing strategies, only 15% of Neurontin sales were for off-label uses. **[Slide 4]** This percentage grew over time as can be seen in a chart that appeared in a study by Michael Steinman, *et. al* in *The Annals of Internal Medicine*. The various shades of green represent prescriptions for non-approved uses. **[Slide 5]** Company documents corroborate Michael Steinman's findings. **[Slide 6]** By 2003, according to one company document, 90% of sales of Neurontin were for off-label uses, uses not approved by the FDA.

[Slide 7] A subsequent study by David Radley and others published in the *Archives of Internal Medicine* found that Neurontin "had the highest proportion of off-label prescriptions" among 160 commonly prescribed drugs and that "only 20% of its off-label use had strong support [for its clinical efficacy] compared with 80% with limited or no support." **[Slide 8]** The study also found that the average off-label usage among commonly prescribed drugs was 21%. Thus, the 2003 company finding that 90% of Neurontin sales were for off-label uses greatly exceeded both the average found by Radley and the Neurontin off-label sales in 1994.

How did Warner-Lambert and Pfizer achieve these off-label sales and maintain them? **[Slide 9]** The answer is that they marketed Neurontin for off-label use.

Warner-Lambert sales representatives encouraged doctors to prescribe Neurontin for a variety of off-label uses even when there was no evidence to support claims of effectiveness or when studies had shown that the drug was not effective.

Warner-Lambert distributed free samples of Neurontin to doctors to encourage them to prescribe Neurontin for off-label treatments for new patients.

[Slide 10] Company documents show that they targeted psychiatrists, who typically would have no reason to use Neurontin for its approved uses.

Warner-Lambert used research and publications to promote unapproved uses for Neurontin, such as neuropathic pain and psychiatric disorders, which Warner-Lambert had determined offered the greatest revenue potential.

Warner-Lambert used outside medical education and communication companies to sponsor research, prepare journal articles on Neurontin and pay researchers to put their names on those articles. These companies were hired to write the articles and find the authors. Articles sponsored by a medical education company tended to report favorable conclusions about Neurontin, but the sponsorship was often not disclosed. Let me remind you that doctors rely on these publications for truthful unbiased information.

Warner-Lambert used these articles and publications as a basis for promoting off-label uses in their sponsored continuing education events. **[Slide 11]** “Medical education drives this market!!” noted one Warner-Lambert business plan. The company used educational activities traditionally considered independent of marketing activities to promote Neurontin for off-label use.

Warner-Lambert recruited physicians who had the potential to influence Neurontin prescribing behavior among their colleagues to serve as speakers in "peer-to-peer selling" programs. These included local champions, who were seen as one of the most effective ways to communicate their message, and "opinion" or "thought leaders," who were influential physicians affiliated with major medical centers. Many of these leaders received substantial payments in honoraria, research grants, or educational grants.

Warner-Lambert conducted teleconferences with paid physician monitors and small groups of physicians. Although presented as educational events, an internal company memo from Carol Ek noted that "the key goal of the teleconferences was to increase Neurontin new prescriptions by convincing non-prescribers to begin prescribing and current prescribers to increase their new prescription behavior."

Warner-Lambert recruited and trained doctors as Neurontin advocates at speaker bureaus. In addition to directly sponsoring medical educational events, Warner-Lambert funded "unrestricted educational grants." Because the grants were "unrestricted," Warner-Lambert officially relinquished control over the program, allowing speakers and participants to discuss unapproved uses of Neurontin and for participants to receive continuing medical education credit, which was not permitted for events directly sponsored by Warner-Lambert. In practice, Warner-Lambert influenced the content as well as the selection of speakers and participants to promote off-label uses of Neurontin. The company also tracked doctors' prescriptions to see if they prescribed Neurontin more after the meetings or after they were hired to speak about the drug.

[Slide 12] Promotion of Neurontin for off-label uses continued and Neurontin prescriptions for unapproved uses increased after Pfizer acquired Warner-Lambert in 2000. Pfizer continued the publication strategy and off-label promotion initiated by Warner-Lambert. Pfizer's marketing and promotional efforts, like those of Warner-Lambert before it, were significant contributing factors to the off-label sales of Neurontin.

Pfizer, like Warner-Lambert, had strong economic incentives to continue promoting off-label uses of Neurontin. Pfizer company documents, business plans and marketing plans reveal that sales for epilepsy were declining and constituted only about 10 percent of all Neurontin sales, that the majority of Neurontin sales were for off-label uses, and that off-label uses for Neurontin presented large attractive markets. Pfizer devoted the majority of its efforts to off-label promotion. Even though approved uses of Neurontin comprised a small percentage of its total sales, Pfizer set and met ambitious goals for Neurontin sales growth that could not reasonably be met by growth in approved uses alone.

Pfizer, in order to meet these goals, continued the publication strategy, continued to suppress and delay publication of clinical studies and data regarding Neurontin's lack of efficacy, and continued to promote articles advocating Neurontin for unapproved uses without disclosing that Neurontin was not effective for those uses. Examples of the suppression and delay in publications of negative clinical studies include the Gorson, POPP and Reckless pain studies, three separate Pfizer studies that did not show efficacy.

Pfizer's marketing plans set out goals for the dissemination of sponsored articles and research to doctors at scientific meetings, conferences, and continuing medical

educational events. To achieve its goals, Pfizer continued to engage outside medical education communications companies to identify and promote "key messages" in articles and presentations about Neurontin.

In summary, Pfizer and Warner-Lambert devoted substantial resources to promoting Neurontin for off-label uses. As the evidence shows their promotional efforts were successful and were significant contributing factors to off-label sales of Neurontin.

Further, even if Pfizer had done nothing to promote off-label uses of Neurontin after it acquired Warner-Lambert, off-label sales of Neurontin would have continued. Successful marketing, in general, and pharmaceutical marketing, in particular, has long term effects. The creation of a successful brand image leads to sales even after promotion stops.

Academic studies confirm that the effects of marketing and promotion are long-lived. Once doctors learn about a drug and are motivated to try it, they tend to remember and stay with the drug.

A study recently published by Dr. Catherine Fullerton and others in *Medical Care* provides further support for my opinion that significant sales of Neurontin would have continued even if Pfizer stopped its off-label promotional activities for Neurontin. Studying Florida Medicaid patients with bipolar disorder, the authors found that: "When new evidence showing [Neurontin] to be ineffective in treating [bipolar disorder] became available and the marketing was discontinued, the rapid growth of [Neurontin] use stopped while the level of its use remained constant."

Not only were their promotional efforts long-lived, they were far-reaching. Off-label marketing of Neurontin directly or indirectly influenced all, or substantially all, doctors prescribing Neurontin.

In addition, the widespread use of Neurontin would further encourage doctors who may not have had direct contact with the drug company to prescribe the drug. According to a study by Professor Ernie Berndt and others "widespread use of a drug may convey information about its safety and efficacy, and, for physicians, may imply 'accepted practice' and hence greater immunity to malpractice lawsuits." As Neurontin sales increased year-over-year, the indirect influences would have become stronger, encouraging physicians to prescribe Neurontin, regardless of whether or not they had direct contact with the company or received sales calls from Neurontin sales representatives.

Given the high levels of detailing, it is unlikely that a doctor would be completely unaware of Neurontin, especially in the specialties where it was most heavily promoted. Neurontin sales representatives visited the majority of primary care physicians, neurologists, rheumatologists, and orthopedists. Since doctors share information and rely on each other for new information, any doctor who did not receive a personal visit would likely learn about Neurontin through a colleague who was visited, that is, through social networking.

Also, because it was perceived as "safe and efficacious", Neurontin was listed on nearly all formularies. Neurontin's formulary status would have also created indirect influences encouraging prescriptions. If a doctor had a patient in need of treatment for one of the numerous off-label conditions, the physician may have prescribed Neurontin

simply because it was on formulary, without ever having been personally contacted by the company or its sales representatives promoting Neurontin.

Thus, the evidence demonstrates that all or substantially all physicians who prescribed Neurontin were directly or indirectly influenced by off-label marketing of Neurontin.

In addition, there is evidence that the suppression of adverse events contributed to increased prescribing of Neurontin. John Marino, Pfizer's Worldwide Team Leader for Neurontin, testified in his deposition before this trial began, that Pfizer has an obligation to share negative results of its exploratory studies with the medical community and that this was the practice at both Warner-Lambert and Pfizer. To suppress or delay a negative study would be misleading and would not present a fair and balanced view, according to Mr. Marino. "The pharmaceutical company's responsibility is to help teach physicians about the risk/benefit profile of appropriate therapies for treatment," including a full explanation of what the risks are, Mr. Marino further testified.

Yet Pfizer allegedly took no affirmative action to disclose what it knew about problems with Neurontin. John Marino admitted that, as far as he was aware of, Pfizer has never sent out a "Dear Doctor" letter to physicians about Neurontin for the treatment of bipolar disorder or any other use.

Having spent considerable time and money communicating positive messages about Neurontin to doctors, Pfizer devoted fewer resources to re-educating doctors when the news about Neurontin was negative. In 2000, Pfizer scientists published results of a negative study showing that Neurontin is not as effective as a placebo in

treating bipolar disorder. But by 2003, the new message about Neurontin's lack of efficacy for treating bipolar patients did not appear to have taken hold among doctors, according to Dr. Gary Sachs, Director of the Harvard Bipolar Research Program at the Massachusetts General Hospital.

Leaving aside the question of whether Pfizer had an affirmative duty to disclose negative information about Neurontin and to disseminate it among doctors, it is clear that withholding or delaying such negative information would cause Neurontin sales for off-label uses to be greater than they would have been if the negative information had been disclosed. Disclosure of negative information may also cause doctors to modify their behavior in other ways, such as more closely monitoring their patients or prescribing an alternative drug, that would lead to better health outcomes.

Doctors would consider this information material to their decisions to prescribe Neurontin and it would have affected their behavior. I understand that although the mode of action of Neurontin was unknown when the drug was originally approved, it is now known that Neurontin depletes serotonin and neuropinephrine and that low levels of these neurotransmitters are an established risk factor for depression and suicide.

Known risks and side effects play an important role in the prescription of drugs. The FDA requires that most risks for drugs be listed on the drug's label or package insert. Doctors take them into consideration when choosing which drug to prescribe for a patient. Drug risks, side effects and adverse reactions with other drugs affect drug sales. Academic studies have shown that an increase in the number of adverse side effects listed on the label reduces the drug's sales or market share, or both. When bad

news about drug side effects or interactions hits the market, sales for that drug typically fall.

Thus suppression of adverse information about Neurontin further enabled Neurontin off-label sales. **[Slide 13]**

In conclusion, based on the evidence, my opinions are:

- The marketing and promotional efforts of Warner-Lambert and Pfizer were significant contributing factors to the off-label sales of Neurontin;
- Significant off-label sales of Neurontin would have continued had Pfizer discontinued off-label promotional activities for Neurontin;
- Pfizer's off-label marketing of Neurontin directly or indirectly influenced all, or substantially, all physicians prescribing Neurontin; and
- Suppression of information regarding serious adverse events enabled growth in off-label sales.